Remarks/Arguments

The foregoing amendments in the claims are of formal nature, and do not add new matter. Prior to the present amendment, claims 39-43 were pending in this application and were rejected on various grounds. The rejection to the presently pending claims are respectfully traversed.

Priority

Applicants rely on the gene amplification assay (Example 92) to establish patentable utility for the claimed antibodies specifically binding the PRO211 polypeptide. The Examiner asserts, without any explanation or supportive scientific arguments or evidence, that Applicants' reliance on this assay "is not persuasive because the assertion of specific, substantial and credible utility of PRO211 as a marker for cancer is found to be unsubstantiated."

It is well established law that the examiner bears the initial burden to present a *prima facie* case that supports his or her rejection of a claim. Only after the examiner has met this burden does the burden of rebuttal shift to the applicant.

Indeed, according to the Utility Examination Guidelines (Federal Register, Vol. 66, No. 4, January 5, 2001) "Any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility. Whenever possible, the examiner should provide documentary evidence regardless of publication date (*e.g.*, scientific or technical journals, excerpts from treatises or books, or U.S. or foreign patents) to support the factual basis for the *prima facie* showing of no specific and substantial credible utility. If documentary evidence is not available, the examiner should specifically explain the scientific basis for his or her factual conclusions."

The Examiner has clearly failed to meet this burden in denying the priority date of September 10, 1998 on the ground that the gene amplification data do not establish patentable utility. In the Office Action mailed on October 2, 2002 (Paper No. 17), the issue of utility based on gene amplification data was not raised. In the present Office Action the Examiner simply dismisses Applicants' voluntarily submitted arguments in support of utility based on the gene

amplification data provided in the specification as "not persuasive," without any attempt to provide any support, either by documentary evidence or scientific arguments, for this conclusion. This is particularly striking, since Applicants' response dated March 14, 2003 was accompanied by an expert Declaration by Audrey Goddard, Ph.D., explaining why based upon the gene amplification results set forth in Table 9 one of ordinary skill in the art would find it credible that the PRO211 polypeptide is a diagnostic marker of human lung and colon cancer, and thus the anti-PRO211 antibodies find utility in the diagnosis of cancer, in particular lung or colon cancer.

The Examiner has failed to provide any explanation or reasoning whatsoever why Dr. Goddard's declaration was deemed insufficient to establish the practical value of the gene amplification data.

Applicants reassert that the present application is entitled to the effective priority date of 10 September, 1998, since the gene amplification results first disclosed in application PCT/US98/18824 establish a specific and credible asserted utility for the anti-PRO211 antibodies claimed. Reasons for this position have been provided in the Amendment and Response dated March 14, 2003, and in the Goddard Declaration. Accordingly, the Examiner is respectfully requested to reconsider her position. Should the Examiner maintain that the utility of the anti-PRO211 antibodies in the diagnosis of cancer is unsubstantiated, she is requested to support this assertion by documentary evidence and/or scientific arguments, and provide Applicants' with appropriate opportunity to rebut.

Claim Rejections – 35 USC §101

6. Claim 39 was rejected under 35 U.S.C. §101 allegedly because the claimed invention was directed to non-statutory subject matter. The Examiner alleges that the claim fails to include any limitations that would distinguish the claimed antibodies from those which occur in nature.

The present amendments to claim 39 that recite "an isolated antibody" should overcome this rejection. According to the specification, an "isolated" antibody is "one which has been

identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step" (See specification, page 76, last line through page 77, line 8).

Thus, the claimed antibodies are distinguished over antibodies in nature and the reconsideration and withdrawal of the present rejection would be in order.

Claim Rejections-35 U.S.C. §112

Claims 39-43 were rejected under 35 U.S.C. §112, first paragraph, since allegedly, the claimed invention was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner alleges that the instant specification as filed fails to describe an antibody that specifically binds to a polypeptide of SEQ ID NO: 2 to the exclusion of binding to any other protein.

Applicants respectfully traverse this rejection.

It is well know to those skilled in the art that antibodies are generally defined in terms of their specific binding to a particular antigen. At the effective filing date of the present application it was well within the skill of an ordinary artisan to raise such antibodies. Thus, techniques for making antibodies were described in Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103, which is reference in and incorporated by

reference into the present application. In addition, the production of antibodies is described in Example 57. Based on this teaching and general knowledge in the art one of ordinary skill had no difficulty at the relevant time frame to make antibodies that specifically bind to a polypeptide of SEQ ID NO: 2. Should the Examiner's arguments be valid, antibody claims could never issue, which is clearly not the law or the practice of the United States Patent Office.

Hence, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections – 112, second paragraph

Claim 39-43 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for recitation of "specifically binds" whose metes and bounds could not be determined from the instant specification because it was unclear if the specificity was defined by binding a specific epitope or to a protein from a particular species or both. Applicants respectfully traverse this rejection.

As discussed above, antibodies are customarily characterized by their ability to specifically bind to a target antigen. In other words, the art-recognized meaning of "specific" binding is that the antibody binds specifically to a particular antigen and does not significantly cross-react with another antigen. Thus the metes and bounds of the claims are well understood by one skilled in the art and accordingly, this rejection should be withdrawn.

Claim Rejections – 35 USC §102

Claims 39-43 were rejected under 35 U.S.C. 102(a) as being anticipated by WO99/58660 because the effective filing date awarded to the instant application was 2/22/00.

As discussed above, the present application is entitled to an effective filing date of 10 September, 1998. Hence, WO99/58660 is not prior art under 35 U.S.C. 102(a).

Hence, Applicants respectfully request that this rejection be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C6).

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: July 21, 2003

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